Substitute for form 1449A/PTO omplete if Known INFORMATION DISCLOSURE Application Numb r 10/667,208 STATEMENT BY APPLICANT (Use as many sheets as necessary) September 19, 2003 Filing Date Carson, Dennis First Named Inventor 1614 **Group Art Unit** Unknown R. Henley JAN 2 2 2004 **Examiner Name** Attorney Docket No: 103.032US1 Sheet 1 of 4

Examiner Initial *	USP Document Number	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	Filing Date If Appropriate
1	US-3,843,681	10/22/1974	Demerson, C. A., et al.	260	326.14 R	06/01/1971
\forall	US-4,337,760	07/06/1982	Rubin, D.	128	1 R	10/31/1979
	US-5,561,151	10/01/1996	Young, J. W., et al.	514	411	01/04/1995
	US-5,811,558	09/22/1998	Adger, B. M., et al.	548	427	04/11/1995
	US-5,939,455	08/17/1999	Rephaeli, Ada	514	547	03/11/1997
1	US-5,955,504	09/21/1999	Wechter, William J., et al.	514	568	03/13/1995
M	US-6,066,741	05/23/2000	Vigano', E., et al.	548	432	09/08/1998
	US-6,545,034	04/01/2003	Carson, et al.	514	411	07/23/1999

FOREIGN PATENT DOCUMENTS							
Examiner Initials	Foreign Document No	Publication Date	Name of Patentee or Applicant of cited Document	Class	Subclass	T²	
W	DE-2226340	03/15/1973	Demerson, Christopher A., et al.	C07D	27/56	Abstract only	
01	EP-0289262	11/02/1986	Venuti, M. C., et al.	C07C	93/00		
-	WO-00/02555	01/20/2000	Nardella, Francis A., et al.	A61K	31/40		
	WO-00/13410	03/09/2000	Monroe, D. A.	H04N	5/76		
 	WO-96/28148	09/19/1996	Wechter, William J., et al.	A61K	31/19		
- h	WO-98/09603	03/12/1998	Wechter, William J., et al.	A61K			
A	WO-98/18490	05/07/1998	Clynes, M. M.	A61K	45/06		

OTHER	R DOCUMENTS NON PATENT LITERATURE DOCUMENTS	
Cite No 1	include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
-	ABRAMSON, S. B., et al., "The Mechanisms of Action of Nonsteroidal	
	Antiinflammatory Drugs", Arthritis & Rheumatism, 32 (1), (Jan. 1989), 1-9	
 	ALEXANIAN, R., et al., "The Treatment of Multiple Myeloma", The New England	
	Lournal of Medicine, 330 (7), (Feb. 17, 1994), 484-489	
	BARLOGIE, B., et al., "Prognostic Factors with High-Dose Melphalan for	
	Refractory Multiple Myeloma.", Blood, 72, (1988), 2015-2019	
 	BATAILLE, R., et al., "Multiple Myeloma", New England Journal of Medicine,	
	336. (1997), 1657-1664	ļ
 	BECKER-SCHARFENKAMP, U., et al., "Evaluation of the Stereoselective	
	Metabolism of the Chiral Analgesic Drug Etodolac by High-Performance Liquid	
	Chromatography", Journal of Chromatography, 621 (2), (Nov. 24, 1993), 199-	
	207	
 	BELLOSILLO, B., et al., "Aspirin and Salicylate Induce Apoptosis and Activation	Lin
	of Caspases in B-Cell Chronic Lymphocytic Leukemia Cells", Blood, 92 (4), (00	W' +)
	Cite	(book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-assue number(s), publisher, city and/or country where published. ABRAMSON, S. B., et al., "The Mechanisms of Action of Nonsteroidal Antiinflammatory Drugs", Arthritis & Rheumatism, 32 (1), (Jan. 1989), 1-9 ALEXANIAN, R., et al., "The Treatment of Multiple Myeloma", The New England Journal of Medicine, 330 (7), (Feb. 17, 1994), 484-489 BARLOGIE, B., et al., "Prognostic Factors with High-Dose Melphalan for Refractory Multiple Myeloma.", Blood, 72, (1988), 2015-2019 BATAILLE, R., et al., "Multiple Myeloma", New England Journal of Medicine, 336, (1997), 1657-1664 BECKER-SCHARFENKAMP, U., et al., "Evaluation of the Stereoselective Metabolism of the Chiral Analgesic Drug Etodolac by High-Performance Liquid Chromatography", Journal of Chromatography, 621 (2), (Nov. 24, 1993), 199-

EXAMINER TO SIDERED 6/15/04

PTC/SB/06A(10-01)
Approved for use through 10/31/2002, OAB 851-0031
US Patent & Trademerk Office: U.S. GEPATHERY OF COALGERGE
on of information unless it contains a valid OAB control number,

Substitute for form 1449A/PTO
INFORMATION DISCLOSURE Complete if Known **Application Number** 10/667,208 STATEMENT BY APPLICANT September 19, 2003 Filing Date (Use as many sheets as necessary) Carson, Dennis First Named Inventor 1614 **Group Art Unit** JAN 2 2 2004 Unknown R. HENIEY **Examiner Name** Attorney Docket No: 103.032US1 Sheet 2 of 4

	OTHE	R DOCUMENTS NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No 1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T'
a		(Aug. 15, 1998), 1406-1414	
- (2) 		BERENDES, U., et al., "Simultaneous Determination of the Phase II Metabolites	
		of the Non Steriodal Anti-inflammatory Drug Etodolac in Human Urine",	
14		Enantiomer, 1, Abstract Only, Chemical Abstracts, Abstract No.	ì
$-\sqrt{2}$			
		126:207064q,(1996), 415-422 BRENNA, E., et al., "New Enzymatic and Chemical Approaches to Enantiopure	 -
į į		BRENNA, E., et al., "New Enzymatic and Chemical Approaches to Enantiopare	ļ
		Etodolac", Tetrahedron, 53, (1997), 17769-17780	
		BROCKS, D. R., et al., "Etodolac Clinical Pharmacokinetics", Clinical	
		Pharmacokinetics, 26 (4), (1994), 259-274	
		CARSON, D. A., et al., "Oral Antilymphocyte Activity and Induction of Apoptosis	
i i		by 2-chloro-2'-arabino-fluoro-2'-deoxyadenosine", Proc. Natl. Acad. Sci. USA, 89	
		(7) (Apr. 1992) 2970-2974	<u> </u>
		CHINETTI G., et al., "Activation of Proliferator-activated Receptors alpha and Y	
		Induces Apoptosis of Human Monocyte-derived Macrophages", The Journal of	
1 1		Biological Chemistry, 273 (40), (Oct. 2, 1998), 25573-25580	
		CUNNINGHAM, D., et al., "High-dose Melphalan for Multiple Myeloma: Long-	1
		term Follow-up Data", Journal of Clinical Oncology, 12, (1994), 764-768	
		DEMERSON, C. A., et al., "Etodolic Acid and Related Compounds. Chemistry	1
		DEMERSON, C. A., et al., Elouolic Acid and Nelated Compounds. Charles	
}		and Antiinflammatory Actions of Some Potent Di- and Trisubstituted 1,3,4,9-	•
i i		Tetrahydropyrano[3,4-b]indole-1-acetic Acids", <u>Journal of Medicinal Chemistry</u> .	
		19 (3), (1976), 391-395	-
		DEMERSON, C. A., et al., "Resolution of Etodolac and Antiinflammatory and	
		Prostaglandin Synthetase Inhibiting Properties of the Enantiomers", <u>J. Med.</u>	
ļ į		Chem., 26 (12), (Dec. 1983), 1778-1780	
		DRACHENBERG, D. F., et al., "Treatment of Prostate Cancer: Watchful Waiting,	
1		Radical Prostatectomy, and Cryoablation", Seminars in Surgical Oncology, 18	
\		(1) (Jan/Feb. 2000), 37-44	<u> </u>
		TRUEEV C. P. et al. "Enhancement of Chemotherapeutic Drug Toxicity to	
1		Human Tumour Cells In Vitro by a Subset of Non-Steroidal Anti-Inflammatory	1
1		Drugs (NSAIDs)", European Journal of Cancer, 34 (8), (July 1998), 1250-1259	
		HAHNFELD, L. E., et al., "Prostate Cancer", The Medical Clinics of North	
}		HAMINFELD, L. E., et al., Prostate Galicer, The Modern Galicer of The Major Major Detient 93 (5) (Sept. 1999) 1231-1245	
		America - The Aging Male Patient, 83 (5), (Sept. 1999), 1231-1245 HAROUSSEAU, J. L., et al., "Double-Intensive Therapy in High-Risk Multiple	
1		HAROUSSEAU, J. L., et al., "Double-intensive Therapy in might-risk widthple	
		Myeloma", Blood, 79 (11), (June 1, 1992), 2827-2833	
		KRAJEWSKI, S., et al., "Detection of Multiple Antigens on Western Blots",	1
l l	1	Analytical Biochemistry, 236 (2), Article No. 0160, (May 1996), 221-228	-
		LANDIS, S. H., et al., "Cancer Statistics, 1998", CA Cancer J. Clin., 48 (1),	İ
	ļ	(1998), 6-29	↓
		LEE, D. H., "Proteasome Inhibitors: Valuable New Tools For Cell Biologists",	-
11		Trends in Cell Biology, 8, (October 1998), 397-403	
	-	LEHMANN, J. M., et al., "Peroxisome Proliferator-activated Receptors alpha and	(01
(3	l	LETIMANN, J. IVI., et al., Peroxisorile Profilerator-activated Neceptors alpha and	<u> </u>

EXAMINER

DATE CONSIDERED

Substitute Disclosure Statement Form (PTO-1449)

*EXAMINER: Initial if reference considered, whether or not disation is in conformance with MPEP 809. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication applicant. I Applicant's unique citation designation number (optional) a Applicant is 10 place a check mark here if English language Translation is attached.

Approved for use through 10/31/2002 OMB 551-0001

MB Penert & Tresement Office: U.S. DEPARTMENT OF COMMERCE
on of Information unless it contains a valid OMB control amount

Substitute for form 1449A/PTO	Complete If Known	
INFORMATION DISCLOSURE	Application Number	10/667,208
STATEMENT BY APPLICANT (Use as many sheets as necessary)	Filing Date	September 19, 2003
OLE S	First Named Inventor	Carson, Dennis
/ =	Group Art Unit	1614
JAN 2 2 2004 💆	Examiner Name	Unknown PHENLEY
Sheet 3 of 4	Attorney Docket No:	103.032US1

	OTHE	R DOCUMENTS NON PATENT LITERATURE DOCUMENTS	
Examiner initials*	Cite No ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	Τ'
M		Y Are Activated by Indomethacin and Other Non-steroidal Anti-inflammatory Drugs", The Journal of Biological Chemistry, 272 (6), (Feb. 7, 1997), 3406-3410	
		LEMAN, EDDY S., et al., "Characterization of the Nuclear Matrix Proteins in a	
1 9 1		Transgenic Mouse Model for Prostate Cancer", <u>Journal of Cellular Biochemistry</u> .	
			İ
		86, (2002), 203-212	
		LEONI, L. M., et al., "Induction of an Apoptotic Program in Cell-Free Extracts by	
}		2-Chloro-2'-deoxyadenosine 5'-triphosphate and Cytochrome C", PNAS, USA,	İ
		95 (16), (Aug. 4, 1998), 9567-9571	
		LOCHMULLER, C. H., et al., "Chromatographic Resolution of Enantiomers	ļ
<u> </u>		Selective Review", Journal of Chromatography, 113 (3), (Oct. 22, 1975), 283-302	
		MARTEL R. R. et al., "Anti-inflammatory and Analgesic Properties of Etodolic	
		Acid in Rats", Canadian Journal of Physiology and Pharmacology, 54 (3), (June	
		1976) 245-248	
		MOONEY P. T. et al., "Cell Pathways' Exisulind 'Aptosyn' Demonstrates	
		Potential to Delay Hormone Therapy in Post-Prostatectomy Men at Risk of	
		Prostate Cancer Recurrence".	
		http://hiz.vahoo.com/bw/000501/ga_cell_pa_1.html, (May 2000), 3 pages	
 		NARDELLA, FRANCIS A., et al., "Enhanced Clearance of Leukemic	
		Lymphocytes in B Cell Chronic Lymphocytic Leukemia (CLL) with Etodolac",	
		Arthritis & Rheumatism, 42 (9) Supplement, Abstract No. 41, (Sept. 1999), page	
		S56	
		RICOTE, M., et al., "The Peroxisome Proliferator-Activated Receptor-Y is a	
		Negative Regulator of Macrophage Activation", Nature, 391, (Jan. 1, 1998), 79-	
		1 •	
		82 RIEDEL, D. A., et al., "The Epidemiology of Multiple Myeloma",	
		Hematology/Oncology Clinics of North America, Multiple Myeloma, 6 (2), (April	
]			
		1992), 225-247	
		ROYALL, J. A., et al., "Evaluation of 2',7'-Dichlorofluorescin and	
		Dihydrorhodamine 123 as Fluorescent Probes for Intracellular H2O2 in Cultured	
		Endothelial Cells", Archives of Biochemistry and Biophysics, 302 (2), (May 1,	
		1993), 348-355	
		SHIFF, S. J., et al., "Nonsteroidal Antiinflammatory Drugs Inhibit the Proliferation	
		of Colon Adenocarcinoma Cells: Effects on Cell Cycle and Apoptosis",	
{		Experimental Cell Research, 222, Article No. 0023,(1996), 179-188	
		TANG, D. G., et al., "Target to Apoptosis: A Hopeful Weapon for Prostate	
		Cancer" The Prostate. (1997), 284-293	
		VAN BREEMEN, R. B., et al., "Characterization of Oxygen-Linked Glucuronides	
1 1		by Laser Desorption Mass Spectrometry", Biomed. Mass Spectrom., 11, Abstract	
		Only Chemical Abstracts, Abstract No. 101:106777c,(1984), 278-283	
-hA		Transfer to Control #00mthonic and Dialogical Evaluation of omega-(N.N.N-	٠,٨
1/1/		trialkylammonium)alkyl Esters and Thioesters of Carboxylic Acid Nonsteroidal (Co	bu4)
<u> </u>	L	I markyrammornum jarkyr Esters and Thiodsters of Garboxyno Total Total Control	

EXAMINER

DATE CONSIDERED

Substitute Disclosure Statement Form (PTO-1449)

- EXAMINER: Initial if reference considered, whether or not citation is in configuration number (optional) 3 Applicant is to place a check mark here if English language Translation is attached

	Under the Paperwork Reduction Act of 1980, no persons are	required to leabour or a conscious of hydricans	
Substitute for form 1449A/PTO	Complete if Known		
INFORMATION DISCLOSURE	Application Number	10/667,208	
STATEMENT BY APPLICANT (Use as many sheets as necessary)	Filing Date	September 19, 2003	
YUSE as many sheets as medasally	First Named Inventor	Carson, Dennis	
/ = ===================================	Group Art Unit	1614	
JAN 2 2 2004 년	Examiner Name	Unknown R. HENCY	
Sheet 4 of 4	Attorney Docket No: 1	03.032US1	

	OTHE	R DOCUMENTS NON PATENT LITERATURE DOCUMENTS	
Examiner Initials*	Cite No 1	include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	τ²
M		Antiinflammatory Agents", Pharm. Res., 6, Abstract Only, Chemical Abstracts, Abstract No. 112:111681y,(1989), 867-873	
		WANG, X., et al., "Antipoptotic Action of 1,25-Dihydroxyvitamin D3 Is Associated with Increased Mitochondrial MCL-1 and RAF-1 Proteins and Reduced Release of Cytochrome c", Experimental Cell Research, 235 (1), Article No. Ex973667 (1997), 210-217	
		WECHTER, W. J., et al., "E-7869 (R-Flurbiprofen) Inhibits Progression of Prostate Cancer in the TRAMP Mouse", Cancer Research, 60, (April 15, 2000), 2203-2208	
		WEISS, H. A., et al., "Aspirin, Non-Steroidal Anti-Inflammatory Drugs and Protection from Colorectal Cancer: a Review of the Epidemiological Evidence", Scandinavian Journal of Gastroenterology, 31 (Suppl. 220), (1996), 137-141	
A		WILEN, S. H., et al., "Strategies In Optical Resolutions", Tetrahedron, 33 (21), Tetrahedron Report Number 38,(1977), 2725-2736	

DATE CONSIDERED 6 EXAMINER Substitute Disclosure Statement Form (FTO-1449)

- EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 809, Draw line through citation if not in conformance and not considered, include copy of this form with next communication to applicant. Applicant's unique citation designation number (optional) 2 Applicant is to place a check mark here if English language Translation is statched